# The molecular dialog between dendritic cells and endometrial microenvironment during equine endometrosis

Dendritic cells (DCs) encompass a heterogeneous family of antigen-presenting cells playing a key role in regulating the inflammatory microenvironment. Nevertheless, a growing body of evidence indicates their involvement, as one of the key players, in the development of tissue fibrosis, as they engage in cross-talk with fibroblasts in response to tissue injury or chronic inflammation. Fibroblasts are the main source of the extracellular matrix (ECM) components which form the structural framework of tissues and organs. They play a crucial role in the pathological fibrotic accumulation of ECM, with collagen type I (COL1) being a predominant deposited ECM component. Consequently, modulation of fibroblast functioning, including their proliferation or differentiation into myofibroblasts, may be important for the progression of fibrotic processes. Given that the molecular basis of the interaction between DCs and fibroblasts is poorly described, this area is in urgent need of further investigation.

Equine endometrosis is a chronic degenerative condition involving endometrial stromal fibrosis along with degenerative changes in the adjacent tissue structures. Results of our study concerning the transcriptomic profiling of mare endometrium at different stages of endometrosis revealed the increased expression of genes related to dendritic cell maturation, which suggests the involvement of these cells in the development of equine endometrial fibrosis. Thus, determining the interactions between dendritic cells and the equine endometrial fibroblasts requires exploration and comprises the main goal of the proposed project.

To meet the project goal, first, the endometrial number of DCs in all stages of endometrosis will be established. Thereafter, in an *in vivo* study DC-dependent changes in ECM remodeling as well as in the transcriptome and proteome of the mare endometrial tissue will be determined. During *in vitro* study, in turn, the impact of DC secretome as well as DC mediators – IL-10 and IL-12 on the transcriptome, proteome, ECM remodeling as well as functional characteristics of equine endometrial fibroblasts during development and course of mare endometrosis will be examined. Finally, the effects of the secretome of endometrial fibroblast obtained at every endometrosis severity stage as well as COL1 on DC maturation and functional characteristics will be studied.

The proposed project ensures a complex and reliable approach to the examined issue. Recognition of all potential factors involved in the cross-talk between DCs and the endometrial microenvironment during mare endometrosis with assessing *in silico* the potential interactions between these molecules will shed more light on the role of DCs in fibrotic processes. The importance of the information gained during the project is difficult to overestimate due to its potential for the prevention and therapy of endometrosis in the mare as well as the improvement of horse husbandry and breeding through the reduction of the financial losses caused by the loss of embryos. In perspective, the results of the project may indicate a new direction in the search for the treatment of fibrotic diseases in humans.